Intro to Proteins II

I. Primary Structure – AA sequence

A. Peptide bonds – covalent N-C bond between two AAs to form a polypeptide

1. Peptide bond backbone is rigid and planar (N and C have sp2 character)

2. The α-carbon is the carbon attached to the R chain

3. Forms with the elimination of water

4. Sequence is always read N🡪C, amino end to carboxylate end

B. Two Primary Components

1. Peptide bond backbone – contains C=O (H acceptor) and N-H (H donor) groups

a. Cis or trans arrangement with respect to α-C positions about peptide bond

b. Generally, trans is favored due to steric clashes of cis

c. Phi (Φ) is the angle of N-C and Psi (Ψ) is the C-C angle

d. Dihedral angle is the measure of rotation about each of the 2 single bonds

i. Ramachandron diagram helps predict folding,

ii. ¾ of configurations are excluded due to impossible sterics

2. Side Chains (R groups) that differ based on AA

C. Disulfide Bonds

1. Covalent Modification

2. Oxidation of two cysteine residues to a cystine

3. Can be inter-chain or intra-chain residues

4. Reduction reactions can separate cystine back to cysteines

D. Protein Size Determinations

1. Average molecular mass of one AA is 110 daltons or 0.11 kD

2. #AA x 110 D = approximate MM of protein (in daltons)

II. Secondary Structure – spatial organization of local AAs

A. Structural predictions based on:

1. Rigidity of peptide bond

2. Restricted set of Φ and Ψ angles

3. Two periodic (regular) structures— α-helix and β-sheets

B. α-helix

1. Tightly coiled backbone with side chains extending outward

a. No steric clashes between residue R chains

b. Right handed coil

2. One turn is approximately 3.6 residues

a. Hydrogen bonding between C=O (n) and N-H (n+4)

3. Supersecondary – Coiled coil

a. Superhelix 🡪 two α-helices coiled around one another

C. β-pleated sheets

1. Looser secondary structure

a. Planar backbone with R groups extending above and below the plane

2. Can run parallel or anti-parallel, depends on direction of N🡪C

a. Parallel – H-bonds are staggered between AAs on opposite strand

b. Anti-parallel – H-bonds directly between AAs on opposite strand

D. Reverse Turns (β-turn, hairpin loop)

1. Causes a bending of the polypeptide chain

2. Stabilized by H-bonding between C=O of residue *i* and N-H of residue *i+3*

3. Reverse turns are usually found on the protein surface

a. Involved with interactions with other molecules

E. Prion Disease

1. Caused by misfolded proteins that act as infectious agents

2. In humans, Creutzfeldt-Jakob Disease

3. Normal prion protein (PrP) is an α-helix, mutated PrP is a β-sheet

a. Creates insoluble protein aggregates

b. Cause of misfolding and normal function of PrP is unknown

III. Tertiary Structure – spatial arrangement of entire polypeptide chain

A. Rules governing tertiary structure:

1. Thermodynamic stability – less energy is more desirable

2. Contribution of each part to overall polypeptide chain folding

a. Electrostatic interactions

b. Covalent bonds and modifications

c. H-bonding

d. Van der Waals (hydrophobic) interactions

B. General Rule

1. Hydrophilic R groups (polar) – outside

2. Hydrophobic R groups (nonpolar) – inside

3. EXCEPTION

a. Channel proteins (porin) is reversed due to the position in the membrane

b. Inner residues are exposed to polar solutes, outer exposed to PM lipids

C. Protein Domains

1. Compact globular regions of a single protein connected by a flexible segment

IV. Quaternary Structure

A. Spatial arrangement of proteins containing more than one protein chain

1. Subunits associate together to form the complete protein

2. Hemoglobin is a tetramer containing 2α and 2β subunits